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Volume 27, Issue 2

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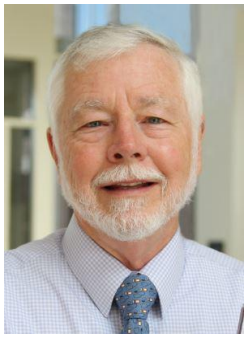
Perspectives: March Madness

By John Wingard, MD



Tonight the NCAA basketball section committee is poised to announce the basketball tournament brackets, and my thoughts turn to March Madness: College basketball's extravaganza with buzzer-beaters, Cinderella teams, and "diaper dandies." The bounces on the court are as erratic as the sharp weather swings outdoors with gentle showers alternating with howling storms.

March has always been a bracing month, punctuated by quirky holidays. Pi Day, followed by National Peanut Butter Lover's Day, and then followed again by National Meatball Day and National Spinach Day. St Patrick's Day. Wellderly Day. National Proofreading Day. Awkward Moments Day. National Goof Off Day, followed by, of course, National I am in Control Day. Who made up these holidays? Then, the month ends aptly with a punctuation mark: April Fool's Day.

This year is no different and is amped up by the wily madness of pandemic. Loss. Fear. Uncertainty. Injustice. Chaos. Those will forever be the descriptors for 2020.

Yet quietly the rhythms of hard work pulsed steadily onward. The CIBMTR effort remained strong in 2020 despite the pandemic. Cumulatively, more than 572,000

cases have been entered into the observational registry with approximately 25,000 new cases added each year. More than 3,600 CAR-T cell infusions have been registered, with greater than 1,000 cases during 2020.

More than 2,800 volunteers pooled their energy and ingenuity and came together in 15 working committees to fuel the CIBMTR research agenda. There are 154 ongoing studies, and 368 new proposals were submitted in 2020. Those proposals were winnowed to 15 finalists, which were presented in the first-ever combined review session during the 2021 TCT Meetings of ASTCT & CIBMTR Digital Experience. Seven were selected by your vote for protocol development. CIBMTR working committee research led to 63 presentations and 89 publications during 2020. Importantly for our future, about 40% were led by early-stage investigators who were paired with senior investigators.

Multiple studies relevant to COVID-19 were launched, and three were published already. The RCI BMT supported 12 studies enrolling 1,400 patients in 2020. The BMT CTN enrolled 1,600 patients in 2020, topping 13,000 cumulative accruals. The CIBMTR continued to support the NHLBI-supported Cure Sickle Cell initiative, contributing data and infrastructure for clinical trials. Five CMS Coverage with Evidence Development studies, designed to extend the reach of transplant to populations not served, continued unabated.

All this work was made possible by uncommon hard work both by CIBMTR staff and all the volunteers who have worked in uncommonly trying times to soldier on in service to our patients. The unheralded dedication of exemplary, highly skilled teams working tirelessly to continue to make a difference in the lives of others reminds us that there were moments of normalcy and decency in 2020.

Resilience. Progress. Teamwork. Those too are apt descriptors for 2020. Do we dare murmur a word like hope? Yes, one can sense the stirrings of optimism. Glimmers of hope that vaccines finally will turn the corner of the pandemic. Yet, madness prevails at the same time with states lifting mask mandates and social distancing measures prematurely, preventive measures that are still needed until vaccines are actually in the arms of all of us. In many ways, the long-awaited rollout of the vaccine is coming at the right season and beckons us to look to a future past March Madness.

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Donor Health and Safety Working Committee

Committee Leadership

Co-Chairs:

- Jack Hsu, MD, University of Florida
- Sandhya R. Panch, MD, MPH, National Institutes of Health (Incoming)
- Nirali N. Shah, MD, National Cancer Institute (Outgoing)
- Galen E. Switzer, PhD, University of Pittsburgh

Scientific Director:

- Bronwen Shaw, MD, PhD, CIBMTR MCW

Statistical Director:

- Brent Logan, PhD, CIBMTR MCW

Statistician:

- Stephanie Bo-Subait, MPH, CIBMTR NMDP

The Donor Health and Safety Working Committee, now in its fifteenth year, comprises a vibrant community of researchers interested in understanding the impact of donation on both related and unrelated hematopoietic stem cell donors. Our committee includes a highly diverse group of individuals interested in the biology, clinical effects / risks, psychosocial experiences, ethics, and policy decisions involved in the donation of stem cells. We are interested in both understanding these issues from a research perspective and in implementing key findings to improve donor safety, experiences, and outcomes.

One of the notable accomplishments of the past few years is the completion of multiple manuscripts from the Related Donor Safety (RDSafe) study. This study was the first large prospective study of related donors. Although RDSafe answered many questions about related donation, study findings also provided fertile ground for future investigations of remaining unanswered questions including those

addressed in an ongoing NIH-funded investigation (NHLBI R01 HL131731) led by Drs. Switzer and Pulsipher focused on health-related quality-of-life among pediatric sibling donors and their families.

Publications from RDSafe to date include:

- Seftel MD, Chitphakdithai P, Miller JP, et al. **Serious adverse events in related donors: A report from the Related Donor Safety Study.** Transplantation and Cellular Therapy. doi:10.1016/j.jtct.2021.01.009. Epub 2021 Jan 15.
- Switzer GE, Bruce JG, Kiefer DM, et al. **Health-related quality-of-life comparison of adult related and unrelated HSC donors: An RDSafe study.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Dec 1; 26(12):2365-2371. doi:10.1016/j.bbmt.2020.08.016. Epub 2020 Aug 20. PMC7686016.
- Pulsipher MA, Logan BR, Kiefer DM, et. al**. Related peripheral blood stem cell donors experience more severe symptoms and less complete recovery at 1-year compared to unrelated donors.** Haematologica. 2019 Apr 1; 104(4):844-854. doi:10.3324/haematol.2018.200121. Epub 2018 Oct 31. PMC6442962.
- Pulsipher MA, Logan BR, Chitphakdithai P, et al. **Effect of aging and predonation comorbidities on the related peripheral blood stem cell donor experience: Report from the Related Donor Safety study.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2019 Apr 1; 25(4):699-711. doi:10.1016/j.bbmt.2018.11.004. Epub 2018 Nov 10. PMC6453753.
- Pulsipher MA, Logan BR, Kiefer DM, et. al. **Higher risks of toxicity and incomplete recovery in 13-17 year old females after marrow donation: RDSafe peds results.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2019 May 1; 25(5):955-964. doi:10.1016/j.bbmt.2018.12.765. Epub 2018 Dec 31. PMC6511296.
- Switzer GE, Bruce J, Kiefer DM, et al. **Health-related quality of life among older related hematopoietic stem cell donors (>60 years) is equivalent to that of younger related donors (18 to 60 years): A Related Donor Safety Study.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2017 Jan 1; 23(1):165-171. doi:10.1016/j.bbmt.2016.10.008. Epub 2016 Oct 14. PMC5182103.
- Switzer GE, Bruce J, Pastorek G, et al. **Parent versus child donor perceptions of the bone marrow donation experience.** Bone Marrow Transplantation. 2017 Sep 1; 52(9):1338-1341. doi:10.1038/bmt.2017.124. Epub 2017 Jun 26. PMC5933883.
- Switzer GE, Bruce J, Kiefer DM, et al. **Health-related quality of life among pediatric hematopoietic stem cell donors.** The Journal of Pediatrics. 2016 Nov 1; 178:164-170.e1. doi:10.1016/j.jpeds.2016.07.009. Epub 2016 Aug 10. PMC5085860.

Additional key publications in the past two years include:

- Panch SR, Logan B, Sees JA, et al. **Shorter inter-donation interval contributes to lower cell counts in subsequent stem cell donations.** Transplantation and Cellular Therapy (in press).
- Seftel MD, Kuxhausen M, Burns L, et al. **Clonal hematopoiesis in related allogeneic transplant donors: Implications for screening and management.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Jun 1; 26(6):e142-e144. doi:10.1016/j.bbmt.2020.02.022. Epub 2020 Mar 5. PMC7440392.
- Farhadfar N, Hsu JW, Logan BR, et al., **Weighty choices: Selecting optimal G-CSF doses for stem cell mobilization to optimize yield.** Blood Advances. 2020 Feb 25; 4(4):706-716. doi:10.1182/bloodadvances.2019000923. Epub 2020 Feb 25. PMC7042992.
- Hsu JW, Shaw BE, Kim S, et al. **Collection of peripheral blood progenitor cells in 1 day is associated with decreased donor toxicity compared to 2 days in unrelated donors.** Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2020 Jun 1; 26(6):1210-1217. doi:10.1016/j.bbmt.2020.02.011. Epub 2020 Feb 20. PMC7347029.
- Wong WH, Bhatt S, Trinkaus K, et al. **Engraftment of rare, pathogenic donor hematopoietic mutations in unrelated hematopoietic stem cell transplantation.** Science Translational Medicine. 2020 Jan 15; 12(526):1-9. doi:10.1126/scitranslmed.aax6249. Epub 2020 Jan 15. PMC7521140.
- Wiener L, Hoag JA, Pelletier W, et al. **Transplant center practices for psychosocial assessment and management of pediatric hematopoietic stem cell donors.** Bone Marrow Transplantation. 2019 Nov 1; 54(11):1780-1788. doi:10.1038/s41409-019-0515-3. Epub 2019 Apr 10. PMC6961459.
- Prokopishyn NL, Logan BR, Kiefer DM, et al. **The concentration of total nucleated cells in harvested bone marrow for transplantation has decreased**

over time. Biology of Blood and Marrow Transplantation: Journal of the American Society for Blood and Marrow Transplantation. 2019 Jul 1; 25(7):1325-1330. doi:10.1016/j.bbmt.2019.01.034. Epub 2019 Feb 2. PMC6615955.

A particular strength of this committee has been to conduct research that may lead to practice-changing guidelines aimed to improve the health and well-being of our donors. A notable example of such a study examined the impact of donor BMI on the collection of GCSF mobilized PBSC from unrelated donors. This study found no benefit in CD34+ yield with increasing GCSF doses in obese and morbidly obese donors and was published in Blood Advances in 2020.

A key ongoing focus of the committee is the effect of cryopreservation on hematopoietic progenitor cell counts. The urgency of this research became even more clear as COVID-19 necessitated that stem cells more frequently be cryopreserved before transport and infusion. Committee co-chair Jack Hsu presented key findings of the effects of cryopreservation on donor grafts and outcomes at the 2020 ASH Annual Meeting. Findings included no statistically significant effect of cryopreservation on engraftment or survival with bone marrow grafts, and slower platelet engraftment, and an increased incidence of chronic GVHD in related donor PBSC grafts. However, with unrelated donor PBSC grafts, cryopreservation was associated with slower engraftment and an increase in non-relapse mortality, relapse, disease-free and overall survivals. It is unclear whether the inferior outcomes are due to cryopreservation or some other factor as cryopreservation was more likely to have been performed for recipients with higher risk profiles. These findings were published in Transplantation and Cellular Therapy in 2021.

The committee would like to particularly recognize the leadership and efforts of Nirali Shah, MD, who was an active co-chair of the committee who provided extremely valuable insights and contributions to the work of our community. Dr. Shah recently stepped down as co-chair of the Donor Health and Safety Working Committee as we welcomed Sandhya R. Panch, MD, MPH, as the newest committee co-chair.

View planned, in-progress, and completed studies and publications on the Donor Health and Safety Working Committee webpage. We encourage participation from the donation and transplant community, especially new members, in ongoing studies or through the submission of new proposals. The committee was encouraged to consider adding a process for performing reviews / expert guidelines alongside the regular study proposals, and a strategic process to do so is in development.

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2021 TCT Meetings | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR

By Tia Houseman

The Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR (TCT Meetings of ASTCT & CIBMTR) are the combined annual meetings of the American Society for Transplantation and Cellular Therapy (ASTCT) and the Center for International Blood & Marrow Transplant Research (CIBMTR). Administrators, clinicians, data managers / clinical research professionals, fellows-in-training, investigators, laboratory technicians, MDs / PhDs, nurses, nurse practitioners, pharmacists, physician assistants, and other allied health professional attendees benefit from a full scientific program that addresses the current issues in HCT and cellular therapy.

Due to the COVID-19 pandemic, the 2021 TCT Meetings of ASTCT & CIBMTR were held virtually as the "2021 TCT Meetings of ASTCT & CIBMTR Digital Experience" instead of in-person in Honolulu, Hawaii. This provided an opportunity for more than 4,600 attendees representing 47 countries in the transplantation and cellular therapy community to continue to receive life-saving education at a time when travel was not an option.

Program Co-Chairs, Ned Waller, MD, PhD, FACP, and Leslie Kean, MD, PhD, along with the Scientific Organizing Committee, put together an excellent program consisting of 6 plenary sessions and 9 concurrent sessions. The ASTCT and CIBMTR teamed up with EBMT and APBMT to present a joint plenary session entitled, "Transplantation and Cell Therapy during Pandemics". NMDP also teamed up with WMDA to present a joint concurrent session— a panel discussion, "Creating Solutions through International Collaboration: Lessons Learned during the COVID-19 Pandemic".

The meetings also included 9 symposia, 13 oral abstract sessions, 12 product theaters, 4 poster highlight sessions, 1 CIBMTR working committee session, 12 ASTCT Educational sessions, 17 Meet-the-Professor sessions (some were repeat sessions), and a Pediatric Day. In addition to an outstanding scientific program, tracks were held for administrative directors, advanced practice providers, clinical research professionals / data managers, information technologists, nurses, and pharmacists.

To view the program as well as recordings, visit the 2021 TCT Meetings of ASTCT & CIBMTR site.

Awards

Lawrence B. Faulkner, MD, received the CIBMTR Distinguished Service Award. The purpose of this award is to recognize individuals who have made outstanding contributions to the CIBMTR's research mission in one or more of the following areas: Promoting HCT research and clinical care in developing countries; advancing the field despite unique challenges; expanding the availability of transplantation; disseminating research results to clinicians and patients to improve outcomes and quality of life; and collaboration with organizations to increase data exchange and research collaboration worldwide.

Hal Broxmeyer, PhD, received the ASTCT Lifetime Achievement Award. This award recognizes an individual who has made continuing contributions to the field of blood and marrow transplantation, either in basic biology or clinical application.

Anthony Fauci, MD, received the ASTCT Public Service Award. This award recognizes an individual outside of the ASTCT membership who has advanced the interests of blood and marrow transplantation or given special service to the patients and families that we serve.

Lectures

Helen E. Heslop, MD, presented the Mortimer M. Bortin Lecture. Her lecture was entitled, "T Cell Immunotherapy via Native and Chimeric Receptors." The Mortimer M. Bortin Lecture commemorates the Founding Scientific Director of the International Bone Marrow Transplant Registry (IBMTR, forerunner of the CIBMTR), whose foresight and dedication was critical to the development of the CIBMTR as a global resource of HCT research. Lecturers are chosen based on their contributions to our understanding of Graft-Versus-Tumor effects and/or the advancement of clinical HCT Research.

Elizabeth J. Shpall, MD, presented the E. Donnall Thomas Lecture. Her lecture was entitled, "Cord Blood: Forerunners and New Horizons." In honor of Dr. Thomas, the E. Donnall Thomas Lecture recognizes an eminent physician or scientist, either a clinician or investigator, who has contributed meritoriously to the advancement of knowledge in blood and marrow transplantation.

Honoring one of our own

Mary Horowitz, MD, MS, was honored during the awards and closing session for 35 years of dedication, devotion, and incredible leadership in the rapidly evolving field of HCT and cellular therapy. In Pavan Reddy's words, Mary is a "sheer force of nature," which is true in so many ways. THANK YOU, MARY!

We hope to see you in Salt Lake City, Utah!

Mark your calendars for February 2-6, 2022, for the Transplantation & Cellular Therapy Meetings of ASTCT & CIBMTR in Salt Lake City, Utah. While it is too early to say exactly what the meeting will look like, attendees unable to travel will still have an opportunity to further their education through the Transplantation & Cellular Therapy Meetings of ASTCT & CIBMTR.

We look forward to seeing you at the Salt Palace Convention Center in February 2022.

Support Opportunities and Additional Information

Questions regarding support opportunities for the 2022 Transplantation & Cellular Therapy Meetings of ASTCT & CIBMTR may be directed to the Conference Office: TCTMeetings@mcw.edu.

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BMT CTN Update

By Amy Foley, MA

CIBMTR & BMT CTN COVID-19 Vaccine Study (CIBMTR SC21-07 / BMT CTN 2101)

In preparation for the BMT CTN State of the Science Symposium (SOSS) held last month, 11 committees were charged with identifying clinical trial concepts addressing the most important issues facing the field. Realizing the impact of the pandemic and the need to know whether vaccines are effective in transplant and cellular therapy patients, the Infection and Immune Reconstitution SOSS Committee presented a draft concept in October for a prospective observational COVID-19 vaccination study. The study will measure anti-COVID-19 antibody levels before and after vaccination. The BMT CTN Steering Committee agreed the study was critically important – but also felt that initiation could not wait until after the Symposium, given the US vaccination timetable. Within 4 months, the BMT CTN formed a protocol team; secured funding from multiple sources secured (including the Be The Match Foundation, the Leukemia and Lymphoma Society, the Multiple Myeloma Research Fund, and the ASTCT); and released the study. This accelerated timeline was possible because of collaboration with the CIBMTR; the study is being done under the CIBMTR's IRB-approved Database and Repository protocols and most clinical data will come from routine CIBMTR data collection. However, the BMT CTN infrastructure is being used for specimen tracking and for supplemental data collection to enhance efficiency and speed of activation. Congratulations go to the SOSS Committee and protocol team for recognizing the unique opportunity to learn more for patients during this infectious disease crisis. More information about the study is available here: CIBMTR SC21-7 / BMT CTN 2101 study

State of the Science Symposium

Thank you for helping to make the 1-day virtual State of the Science Symposium a resounding success! A special thank you to the >150 committee members who volunteered many hours to assess the current landscape and propose studies to fill the gaps and to the external reviewers who provided constructive feedback resulting in strengthened concepts.

About 450 attendees tuned in to hear the Committees Chairs present 15 study concepts. Attendees asked many questions (>200 submitted and answered during the sessions!) and scored the concepts via survey after the symposium. Committee Chairs and the BMT CTN leadership team met the day after to review the scores and prioritize the top studies. These 2021 priority concepts will serve as a road map for future trials using the resources of the BMT CTN, NCI Cooperative Groups, and other programs. A manuscript regarding the SOSS is in progress and is expected to be available later this year. In the meantime, the presentations are available for access here: BMT CTN SOSS

About the BMT CTN

The CIBMTR shares administration of the BMT CTN Data and Coordinating Center with NMDP/Be The Match and The Emmes Company. Together, these three organizations support all BMT CTN activities.

To receive up-to-date information about BMT CTN studies, meetings, and news:

Like us on Facebook: facebook.com/BMTCTN

Follow us on Twitter: twitter.com/BMTCTN (@BMTCTN)

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RCI BMT Update

By Erin Leckrone, MBA

NMDP and the CIBMTR are excited to announce NMDP IRB approval of their new ACCESS clinical trial protocol, titled, "A multicenter Phase II trial of HLA-mismatched unrelated donor hematopoietic cell transplantation with post-transplantation cyclophosphamide for patients with hematologic malignancies."

ACCESS will assess whether transplantation of a PBSC or bone marrow product from a (HLA) mismatched, unrelated donor (MMUD) using post-transplant cyclophosphamide (PTCy) based GVHD prophylaxis will be safe and feasible and result in a high likelihood of overall survival at one year after HCT.

ACCESS will have three patient groups—two adult and one pediatric—totaling as many as 180 patients. Patients eligible for ACCESS are those who do not have an available HLA-matched sibling or unrelated donor and will receive a MMUD PBSC or bone marrow (pediatric group only) product at one of the approximately 40 participating transplant centers. The study is expected to span three years—two years of enrollment and one year of follow-up.

The ACCESS trial is a follow-up study to the recently completed NMDP/Be The Match-sponsored prospective multicenter Phase II study, called 15-MMUD, that assessed MMUD transplantation using PTCy with bone marrow grafts. That trial successfully met all of the study objectives, with high rates of overall survival and engraftment coupled with a low incidence of severe acute GVHD. Almost 50% of the patients enrolled in that trial were racial / ethnic minorities who did not have an available well-matched donor in the family or on the registry. Many of these patients would not have had a transplant were it not for the availability of the clinical trial.

The ACCESS trial will expand the reach of this approach because the clear majority of allogeneic transplants for adult patients use PBSC grafts. The ACCESS protocol will also explore the safety and efficacy of MMUD bone marrow in pediatric patients with hematological malignancies who lack well-matched family and unrelated donor options. The ACCESS trial is another step toward the NMDP/Be The Match goal of democratizing cell therapy and ensuring that access to a suitable donor is no longer a barrier to transplant.

"Our success with the 15-MMUD study provides compelling evidence that a treatment approach using mismatched unrelated donors is a strong option for patients who don't have an HLA matched, unrelated donor—most of whom are from diverse racial or ethnic backgrounds," says Steven Devine, MD, NMDP protocol chair for the ACCESS trial and Chief Medical Officer at Be The Match. "Our efforts aim to achieve a likelihood of a donor match for close to 100% of patients—unprecedented access to a quality donor for everyone."

Transplant is a well-established potentially curative therapy for hematological diseases, and the best outcomes occur in the setting of a well-matched family or unrelated donor.

"Unfortunately, only 30% of patients will have a well-matched family donor, and only 19-75% a well-matched unrelated donor," says Bronwen Shaw, MD, PhD, protocol officer for the ACCESS trial and Chief Scientific Director at CIBMTR MCW. "There is no doubt that patients from racial / ethnic minorities are disproportionately disadvantaged in transplant medicine. This creates a critical

need to develop strategies for safe, effective transplant using mismatched donors to expand access to this potentially curative therapy to all patients in need."

"The use of PTCy in mismatched unrelated donor transplantation effectively expands transplant access to racial and ethnic minorities. Serving a large population of Hispanic patients, access to this platform allows our program to identify a suitable donor for every patient we evaluate," says Antonio Martin Jiménez Jiménez, MD, Network transplant center chair, University of Miami, Sylvester Comprehensive Cancer Center.

The ACCESS protocol is expected to enroll as many as 180 patients between August 2021 and August 2023. Patients will be followed for one-year post-transplant.

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Health Services Research Update

By Jaime Preussler, MS; Lih-Wen Mau, PhD, MPH; Christa Meyer, MS; Tatenda Muptuaze, PhD; Jennifer Sees, MPH

The Health Services Research Program uses administrative claims data to study and estimate patterns of costs and use of cellular therapies. The team currently has administrative claims data from CMS (Medicare data from 2010- 2016, and Medicaid data from 2010-2014). These data are linked with CIBMTR registry data and contain information on reimbursement, service utilization, and overall survival. The linked CIBMTR-CMS dataset allows for the inclusion of more comprehensive patient-, disease-, and transplant-related characteristics than either dataset provides alone.

Studies in progress that use these data will examine:

- Prevalence of complications, health care utilization, and costs among patients with sickle cell disease enrolled in Medicaid between 2010 and 2014;
- Trends in utilization of allogeneic HCT among patients with AML enrolled in Medicare or Medicaid from 2010-2016.

For more information about the Health Services Research Program, visit the Health Services Research webpage or email Jennifer Sees.

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Bioinformatics Research: How better collection of race and ethnicity information can improve matching for HCT

By Abeer Madbouly, Principal Bioinformatics Scientist

Matching patients in need of HCT with available donors is a multi-faceted process that is influenced by many variables, including the donor and patient's geographical ancestry. Self-identified race and ethnicity, although predominantly a social construct, has been frequently used in healthcare as an indicator for genetic and geographical roots. While similar race and ethnicity for both the patient and donor does not directly impact the outcomes of transplant, the odds are much higher for a patient to find an HLA-matched donor of the same ethnic roots.

In the diverse Be The Match registry, it is crucial that the self-identified race and ethnicity information properly reflect a donor's geographical ancestry. This information plays a key role in resolving HLA typing ambiguities for legacy donors. Inaccurately represented donor populations can lead to errors in the list of potentially matched donors provided to a patient searching the registry, particularly for patients of color. The Bioinformatics Research team analyzed the impact of self-identified race and ethnicity on projected matches and investigated how well we match for multiple groups of donors on the registry.

We studied a group of 99,000 donors who were projected to be potential matches for searching patients between the years 2000 and 2014. Right off the bat, we detected notable disparities in the quality of recruitment HLA typing for multiple donor race groups. Due to the older donor recruitment timeframe, more than 50% and 70% of donors lacked HLA-C and DQB1 typing respectively. These are HLA genes crucial for matching. Larger disparities were found in African-American (AFA), Hispanic (HIS), and Asian or Pacific Islander (API) donors who lacked around 70% of HLA-C and 85% of HLA-DQB1 typing. This meant that our matching algorithm, HapLogic, had to fill these HLA gaps using its built-in statistical imputation methods, requiring accurate self-identified race and ethnicity information for these donors. Figure 1 shows the gaps in HLA recruitment typing for our study dataset by broad race group.

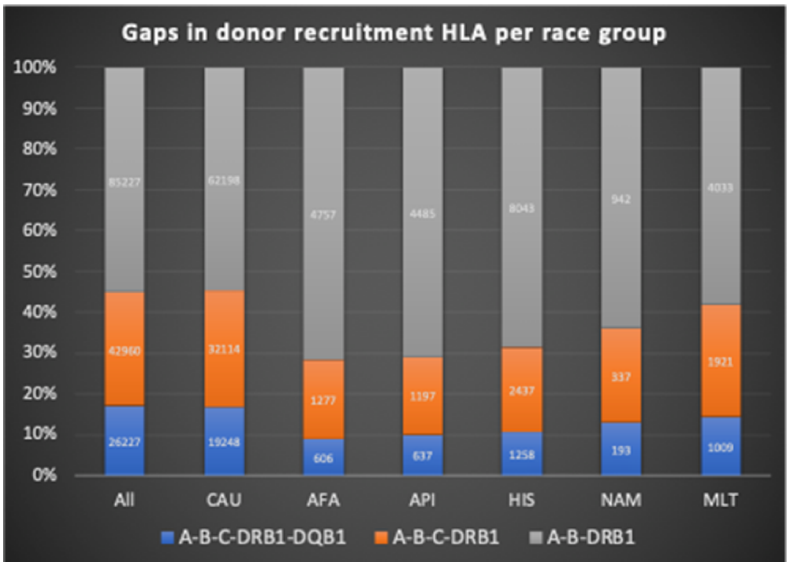

Figure 1: Disparities in donor typing in the study cohort by self-identified race and ethnicity, AFA: African-American, API: Asian or Pacific Islander, CAU: European Caucasian, HIS: Hispanic, MLT: Multi-ethnic, NAM: Native-American.

Comparing the projected matching results with high-resolution confirmatory typing of the donors, we found that African-American donors had the highest matching error of about 9%. This means that, for our study dataset, HapLogic could not find the correct match 9% of the time, when a donor (and likely the patient) was African-American.

Digging deeper, we observed that self-identified race and ethnicity groups demonstrating higher error in matching tended to include subgroups that share a common continental origin, such as African Black (referring to individuals with African roots) or South and Central American Hispanic (representing the majority of Latin America). These groups can be split in a way that would better reflect the genetic identity of these donors and avoid confounding in predictions caused by mixing too many genetically distinct race groups. Based on these findings, Be The Match started using a new recruitment form in July 2020. Thousands of donors have already been recruited using this new form. As we accumulate data on these new donors, we plan to conduct detailed population genetics analyses to compare the old and new categorizers and identify specific areas of improvement for more accurate match predictions, with a specific focus on our underserved communities.

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Immunobiology Research study describes the effect of HLA mismatching detected at higher resolutions on unrelated donor HCT outcomes

By Cynthia Viera-Green, Principal Immunobiology Research Scientist

The gold standard for matching is either an 8/8; pairs of alleles for HLA-A, -B, -C, -DRB1 all matched; or 10/10 where HLA-DQB1 is taken into account. More recently, matching for HLA-DPB1 is beneficial. For HLA-A, -B, -C (class I), exons 2 and 3 are sequenced; for HLA-DRB1, -DQB1, -DPB1 (class II), exon 2 alone is sequenced. Typing of the antigen-recognition domain defined by these regions is called "high resolution" typing. HLA typing technology had changed little in the last 10 years until the introduction of so-called next-generation sequencing techniques.

Recently several studies have shown a potential beneficial impact of matching for regions outside the antigen-recognition domain considering almost the entire gene. The hyper-polymorphic nature of the HLA region along with limitations in sequencing technology previously prevented laboratories from achieving full gene resolution typing. A new next-generation sequencing system called ultra-high resolution expands coverage to full gene for class I loci and exons 2 and 3 in class II loci. The Immunobiology Research Program began using these techniques for the retrospective typing program utilizing stored donor and recipient samples in the CIBMTR Research Repository several years ago.

With this expanded information, the Immunobiology Working Committee study IB19-01a examined the "Impact of previously unrecognized HLA mismatches using ultra high-resolution typing in unrelated donor hematopoietic cell transplantation." No associations were found between ultra-high resolution mismatching and overall survival among transplants equivalently matched (10/10) based on conventional

high-resolution matching standards. Consideration of ultra-high resolution differences among equivalently matched donor options may reduce the risk of grades II-IV acute GVHD and in some cases, transplant-related mortality. Since the primary outcome of overall survival was not altered by ultra-high resolution, the results suggest that the majority of HLA polymorphism is captured in the current high-resolution matching standard. However, the study also suggests that more research is needed to better understand the influence of ultra-high resolution matching in respect to GVHD risk. The resulting manuscript was recently accepted for publication in the Journal of Clinical Oncology.

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2021 TCT Meetings of ASTCT & CIBMTR: Clinical Research Professionals /Data Management Track

By Eileen Tuschl

We had a great turnout for our first Virtual Clinical Research Professionals / Data Management meeting at the 2021 TCT | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR Digital Experience. Our meeting took place February 1-4 from 10 am – 2 pm CST daily, with an average of 520 data professionals attending each day. The digital platform allowed 250 more data professionals to attend this year.

Speaker highlights included: Hot Topics – COVID, HCT Product & Infusion, Consent and You - What it All Means, HLA Barriers in Mismatched Unrelated Donor Transplants, Chronic GVHD, Conditioning Intensity, and Immune Deficiencies.

Laurian Walters and Claudette Edwards received this year's award for best oral abstract for their presentation titled, "Building a Data Management Training Program for Initial Hiring, Onboarding, and Ongoing Competency".

Additional oral abstracts included:

- "Leveraging Lean Management Systems (LMS) to Transform a Blood and Marrow Transplant Data Management Program" presented by Madhu Ragupathi.
- "Use of a Business Intelligence Tool for Multicentric Analysis in Hematopoietic Stem Cell Transplantation in Brazil with Data Extracted from the Data Back to Center – CIBMTR" presented by Anderson Simione.

Presentation PowerPoints can be found on the *2021 Clinical Research Professionals / Data Management* page.

Special thanks to all who completed their evaluations! We use these data to improve our meetings from year to year.

2021 TCT Meetings of ASTCT and CIBMTR: New Data Manager Onboarding Track

CIBMTR Data Operations offers new data manager onboarding twice a year. In-person each February at the TCT | Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR and each September virtually.

New Data Manager Onboarding is for individuals with 6 months or less experience at their center. The classes include interactive training in our FormsNet3 training environment and CIBMTR Portal along with topics that are pertinent to new data managers to submit quality data.

February 15-19, we held new data manager virtual onboarding sessions for 36 data managers. Topics presented included: Resources for Data Managers, introduction to the CIBMTR Portal, forms journey, CPI / CTA, CDVR / TCSA / Queries, and a guide to the audit process.

Our next class will take place in September 2021. Registration will open in July 2021 and will be limited to 35 participants.

The TCT® Trademark belongs to the Cardiovascular Research Foundation. ASTCT, CIBMTR, MCW, NMDP, the 2019, 2020, and 2021 TCT Conferences and materials are NOT affiliated with or sponsored by Cardiovascular Research Foundation.

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Sharing Your Research with the Public

By Jennifer Motl

These five new plain-language summaries may help your patients:

People who had a blood or marrow transplant (BMT) have higher risk dying from COVID-19

Largest study so far shows that most patients survive

Read more: accessible or 1-page version

Changes keep BMT safe and available during pandemic

Be The Match Registry® overcomes COVID-19 challenges

Read more: accessible or 1-page version

CAR-T therapy for lymphoma, leukemia, works well

Large study of tisagenlecleucel shows it helps hard-to-treat cases

Read more: accessible or 1-page version

New scoring tool helps children and teens with leukemia

Tool forecasts how well blood and marrow transplant will work

Read more: accessible or 1-page version

New treatment may help more people have a safe donor match for blood and marrow transplant

Use of cyclophosphamide after BMT expands access for people of color

Read more: accessible or 1-page version

On the Study Summaries for Patients webpage, you will find even more summaries.

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Additional Research Datasets Available for Secondary Analysis

By Liz Siepmann

In accordance with the NIH Data Sharing Policy and NCI Cancer Moonshot℠ Public Access and Data Sharing Policy, the CIBMTR is making publication analysis datasets publicly available on the CIBMTR Research Datasets for Secondary Analysis webpage.

These publication analysis datasets are freely available to the public for secondary analysis. While providing these data, the CIBMTR is committed to safeguarding the privacy of participants and protecting confidential and proprietary data.

NEW datasets are now available online.

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Our Supporters

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Abbreviations

Need an acronym defined? Review our list of common abbreviations.

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CIBMTR® is a research collaboration between the National Marrow Donor Program (NMDP)/Be The Match and Medical College of Wisconsin.

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CIBMTR® (Center for International Blood and Marrow Transplant Research®) is a research collaboration between the National Marrow Donor Program®/Be The Match® and the Medical College of Wisconsin